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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/674,752	01/11/2001	Johannes Jacobus Voorberg	294-86	5298
7590	09/11/2007			
Ronald J Baron Hoffmann & Baron 6900 Jericho Turnpike Syosset, NY 11791			EXAMINER HADDAD, MAHER M	
			ART UNIT 1644	PAPER NUMBER
			MAIL DATE 09/11/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

09/674,752

Applicant(s)

VOORBERG ET AL.

Examiner

Mahe M. Haddad

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1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 July 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) 87 and 89-100 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 87, 89 and 91-100 is/are rejected.
- 7) ☒ Claim(s) 99 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 7/12/07, is acknowledged.
2. Claims 87 and 89-100 are pending and under examination in the instant application.
3. In view of the amendment filed on 7/12/07, only the following rejections are remained.
4. For clarity it is suggested that the preamble of claims 87, 89-87 and dependent claims thereof be change to recite "an isolated antibody" instead of an isolated polypeptide.
5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 87, 89, 91-100 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated **antibody** capable of specific binding to factor VIII and comprising a heavy chain variable region of a human antibody with factor VIII specificity and a light chain variable region of a human antibody, wherein the heavy chain variable region comprises a sequence selected from the group consisting of SEQ ID NO: 23, SEQ. ID. NO: 25, SEQ. ID. NO: 32, SEQ. ID. NO: 34, SEQ. ID. NO: 36, SEQ. ID. NO: 38, SEQ. ID. NO: 49, and SEQ. ID. NO: 51, and a composition thereof does not reasonably provide **enablement** for an isolated polypeptide capable of specific binding to factor VIII and comprising a heavy chain variable region of a human antibody with factor VIII specificity and a light chain variable region of a human antibody, wherein the heavy chain variable region comprises a sequence selected from the group consisting of SEQ ID NO: 27, 28, in claims 87, 89-90 or the compositions in claims 98-100. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with this claim for the same reasons set forth in the previous Office Action mailed 3/8/07.

Applicant's arguments, filed 7/12/07, have been fully considered, but have not been found convincing.

Applicant submits that only the heavy chain is critical for the activity of the antibody, i.e., the light chain can be varied without affecting the activity of the antibody. Applicant submits that, Examples 2, 8 and 9 of the specification describe the isolation of factor VIII binding scFv from phage display libraries for which the variable heavy chain is derived from the immunoglobulin repertoire of a patient with hemophilia A; but the variable light chain is derived from the vector PHEN-VLrep, which contains a variable light chain repertoire of non-immune source. Figures 1, 2, 8 and 10 show that functional factor VIII binding scFv can be isolated using this protocol. Thus, the specification clearly demonstrates that light chain repertoires derived from non-

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immunized donors can be used to isolate antigen-specific scFv when combined with a variable heavy chain repertoire of hemophilia A patients with inhibitory antibodies.

However, instant SEQ ID NO: 27 (EL-5) and SEQ ID NO: 28 (EL-25) comprises only the FR1, CDR1, FR2, CDR2 and FR3 but not the CDR3 and FR4 (see Figure 4B). These heavy chain variable region sequences that lack the CDR3-FR4 would not bind factor VIII and cannot be used with any variable light chain to provide functional antibody.

Regarding claims 98-100, while Applicant now claiming a composition, however, the claims still recite the *in vivo* intended use "for the treatment of factor VIII inhibition in a human individual". Accordingly, the rejection is maintained for reasons of record.

6. Claim 90 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and recite "an isolated antibody" in the preamble of claim 90.

7. No claim is allowed.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).


A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

August 31, 2007



Maher Haddad, Ph.D.
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